REMARKS

The Official Action mailed 1 October 2002, has been received and its contents carefully noted. Claims 1-16 were rejected. By the present communication, claims 1-16 have been cancelled and claims 17-31 have been added to define Applicant's invention with greater particularity. Claims 17-31 will be pending upon entry of the amendments herewith. The added claims add no statutory new matter, being fully supported by the specification and original claims as filed. The new claims are believed to place the application in condition for allowance. Therefore, entry of the amendment and reconsideration is respectfully requested.

Rejection under 35 U.S.C. 102(e)

Claims 1-3, 9, 10-12, and 15 were rejected under 35 U.S.C.102(e)[1], as allegedly being anticipated by Chan et al. U.S. Patent No. 6,275,726 B1 ("the '726 patent" or "Chan"). Specifically, the Examiner deemed that Chan et al. disclose "a method of delivering a clarifying agent past a surface permeability layer of skin to a covered biological tissue to enhance optical transparency".

As amended herein, claims 1-16 have been cancelled, thereby mooting the present rejection of claims 1-3, 9, 10-12, and 15 under 35 U.S.C. 102(e). Nevertheless, Applicant respectfully submits that new claims 17-31 are not anticipated by Chan and, thus, are patentable under 35 U.S.C. 102(e).

In particular, claims 17-23 are directed to a method for enhancing the optical transparency of a covered biological tissue which comprises contacting the surface permeability barrier with a clarifying agent and applying a driving force to the barrier to deliver the clarifying agent to the biological tissue covered by the surface permeability barrier. The driving forces of iontophoresis, electroporation, physical and chemical forces, and acoustic and optical pressure are recited in dependent claims 18-20.

Chan et al. do not disclose a method for enhancing the optical transparency of a biological tissue wherein a driving force is used to cause the clarifying agent to bypass the surface permeability barrier, as is recited in pending claims 17-23. At most, Chan et al. disclose that delivery of "replacement fluid" can be by injection or by removal of all or a portion of the

epidermis. *See e.g.*, '726 patent, col. 3, line 64 to col. 4, line 1. Because Chan et al. do not teach each and every element of claims 17-23, Chan et al. does not anticipate claims 17-23.

Claims 24-29 are directed to a method for enhancing the optical transparency of a biological tissue which comprises contacting the surface permeability barrier with a clarifying agent and an enhancing agent to deliver the clarifying agent to the biological tissue covered by the surface permeability barrier to a greater extent than would occur in the absence of the enhancing agent. Specific types of enhancing agents are recited in dependent claims 25-26.

It is noted that Chan et al., at most, discloses that delivery of "replacement fluid" can be by injection or by removal of all or a portion of the epidermis. Chan et al. do not disclose that a permeability enhancing agent can be used to deliver a clarifying agent to a tissue underlying a surface permeability barrier, as recited in the present claims. Because Chan et al. do not teach each and every element of claims 24-29, Chan et al. do not anticipate claims 24-29.

Claims 30 and 31 are directed to a method for enhancing the optical transparency of skin which comprises breaching at least one layer of the stratum corneum overlying such skin by a method selected from the application of sonophoresis, insertion of a microneedle array, surgical removal, radiofrequency generator-induced ablation or electrical arcing-induced ablation. Chan et al. do not disclose such a method, in part because Chan et al. make no mention whatsoever that the methods of sonophoresis, use of a microneedle array, and ablation by use of a radiofrequency generator or electrical arcing can be used to remove at least one layer of the stratum corneum. Accordingly, Chan et al. do not anticipate claims 30-31.

For the reasons stated above, Applicant respectfully submits that present claims 17-31 are patentable under 35 U.S.C. 102(e) in light of Chan et al.

Rejection under 35 U.S.C. 103(a)

Claims 4-8 and 13 were rejected under 35 U.S.C. 103(a), as allegedly being unpatentable over Chan et al. as applied to claim 1 above, and further in view of Edwards, U.S. Patent No. 5,833,647 (Edwards). Claims 7 and 14 were rejected under 35 U.S.C. 103(a), as being unpatentable over Chan et al. as applied to claim 1 above, and further in view of Weaver et al. U.S. Patent No. 5,019,034 (Weaver et al.). Claim 16 was rejected under 35 U.S.C. 103(a), as

[1] Although the Office Action states that the rejection is under 35 U.S.C. 102(b), the Examiner clarified that

being unpatentable over Chan et al. as applied to claim 1 above, and further in view of Henry, et al., J. Pharm. Sci. 87(8):992-925 (Henry et al.).

As amended herein, claims 1-16 have been cancelled, thereby mooting the present rejection of claims 4-8, 13, 14, and 16 under 35 U.S.C. 103(a). Nevertheless, Applicant respectfully submits that new claims 17-31 are not obvious in light of Chan et al. and Edwards, Chan et al. and Weaver et al., or Chan et al. and Henry et al.

Chan et al. and Edwards

Of the new claims submitted in the present amendment, claims 18, 19, and 30 are most closely related to cancelled claims 4-8 and 13, which were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Chan et al. as applied to claim 1 above, and further in view of Edwards. Claim 17, and claims 18 and 19 dependent therefrom, are directed to a method for enhancing the optical transparency of a biological tissue which comprises contacting the surface permeability barrier with a clarifying agent and applying a driving force to the barrier to deliver the clarifying agent to the biological tissue covered by the surface permeability barrier. The driving forces of iontophoresis, electroporation, physical and chemical forces, and acoustic and optical pressure are recited in claim 18; the driving forces of a temperature gradient and concentration gradient are recited in claims 19 and 20, respectively. Claim 30 is directed to a method for enhancing the optical transparency of skin comprising breaching at least one layer of the stratum corneum overlying such skin by a method selected from the application of sonophoresis, insertion of a microneedle array, surgical removal, and radiofrequency generator-induced ablation or electrical arcing-induced ablation.

As noted by the Examiner, Chan et al. do not disclose methods for enhancing the optical transparency of a biological tissue wherein a driving force delivers the clarifying agent past the surface permeability barrier. At most, Chan et al. disclose that delivery of "replacement fluid" can be by injection or by removal of all or a portion of the epidermis. *See e.g.*, '726 patent, col. 3, line 64 to col. 4, line 1. The Examiner deemed that Edwards teaches the use of sonophoresis, electroporation, temperature gradient, and iontophoresis as methods to deliver drugs to a patient. The Examiner alleges it would have been obvious to one of ordinary skill in the art at the time of

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the rejection was meant to be under 35 U.S.C. 102(e).

the present invention to use the therapeutic drug delivery teachings of Edwards in the light attenuation reduction method of Chan et al., in order to effectively deliver a medicament transdermally.

Applicants respectfully submit that the Chan et al. and Edwards disclosures address two different problems and deliver agents for two different purposes. Edwards is directed to a method of enhancing transport of a therapeutic drug, *i.e.*, vasopressin, calcein, insulin, from a drug-containing hydrogel or lipogel that serves as a carrier for the drug during transdermal delivery. Nowhere does Edwards disclose that its method could be used for the non-therapeutic delivery of an agent to improve optical properties of a tissue, such as delivery of a clarifying agent according to the present invention. The disclosure of Chan et al. focuses on transient replacement of an intracellular fluid with a biocompatible fluid for the purpose of temporarily reducing light attenuation in the tissue. Applicant respectively submits that neither Chan et al. nor Edwards provides any suggestion that would motivate one of ordinary skill in the art to combine these two disclosures to reach the presently claimed invention with a reasonable likelihood of success. Because neither Edwards nor Chan et al. provides the motivation requisite under 35 U.S.C. 103(a) for one of skill in this art to combine one reference with the other, Applicant submits that the present claims are patentable under 35 U.S.C. 103(a) in view of Chan et al. and Edwards.

Chan et al. and Weaver et al.

Of the new claims submitted in the present amendment, claims 18 and 25 are most closely related to cancelled claims 7 and 14, which were rejected under 35 U.S.C. 103(a), as being unpatentable over Chan et al. as applied to claim 1 above, and further in view of Weaver et al. Claim 18 depends from claim 17, discussed above, and addresses a driving force of optical pressure. Claim 25 depends from independent claim 24, which is directed to a method for enhancing the optical transparency of a biological tissue comprising contacting the surface permeability barrier with a clarifying agent and an enhancing agent to deliver the clarifying agent to the biological tissue to a greater extent than would occur in the absence of the enhancing agent. Claim 25 recites that the enhancing agent can be a penetrating solvent.

The Examiner deemed that Chan et al. disclose the claimed invention except for using optical pressure and solvent to deliver the agent. The Examiner deemed that Weaver et al. teach the use of optical pressure to drive molecules across skin barrier and penetrating solvents to increase skin permeability. The Examiner alleges it would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Weaver et al. in the invention of Chan et al. in order to effectively deliver fluids past the skin barrier.

Applicant respectfully submits that the deficiencies of Chan et al. with respect to claim 18 are discussed above. Regarding claim 24, and its dependent claim 25, Chan et al. do not disclose that a clarifying agent can be delivered to a tissue underlying a surface permeability barrier through use of a permeability enhancing agent. Weaver et al. is primarily directed to a method of using electroporation and/or iontophoresis to deliver drugs transdermally; delivery using optical pressure and an enhancing agent also are disclosed. The Examiner has not pointed to any teaching or suggestion in Weaver et al., and Applicant can find none, that would motivate one of ordinary skill in the present art to consider using the Weaver et al. teachings in a method for reducing light attenuation of a tissue, which is the focus of Chan et al. The two disclosures are directed to two entirely different objectives, *i.e.*, transdermal drug delivery and delivery of a temporary replacement fluid to a tissue to reduce light attenuation therein, respectfully. This difference, and the absence of any express suggestion in either reference that the Chan et al. method could be modified to include optical pressure and an enhancing agent, supports Applicant's submission that one of skill in this art would not be motivated to combine the two teachings to reach the presently claimed invention with a reasonable likelihood of success. Thus, Applicant submits that the pending claims are patentable under 35 U.S.C. 103(a) in view of Chan et al. and Weaver et al.

Chan et al. and Henry et al.

Of the new claims submitted in the present amendment, claim 30 is most similar to cancelled claim 16, which was rejected under 35 U.S.C. 103(a), as being unpatentable over Chan et al. as applied to claim 1 above, and further in view of Henry et al. As outlined above, claim 30 focuses on a method for enhancing the optical transparency of skin comprising breaching at least one layer of the stratum corneum overlying such skin by a method selected from the application

of sonophoresis, insertion of a microneedle array, surgical removal, and radiofrequency generator-induced ablation or electrical arcing-induced ablation.

The Examiner deemed that Chan et al. disclose the invention in cancelled claim 16 except for delivering the agent using needles to increase the skin permeability. The Examiner deemed that Henry et al. disclose using microneedles to increase skin permeability. The Examiner alleges it would have been obvious to one or ordinary skill at the time of the invention to use the teachings of Henry et al. in view of Chan et al. in order to effectively deliver molecules across the skin barrier.

Applicant respectfully submits that the deficiencies of Chan et al. with respect to claim 30 are outlined above. Henry et al. describe the use of microneedles to transdermally deliver a drug past the stratum corneum to the viable epidermis, where it then diffuses through the deeper dermal tissue and is systemically delivered. *See* Henry et al. page 922, col. 2, paragraphs 1 and 2. This delivery strategy is different from that of Chan et al., which teaches injection of replacement fluid directly into the dermis layer ('726 patent, col. 3, lines 64-66) for localized (not systemic) delivery. Thus, the objectives of Henry et al. and Chan et al. are completely different. The disclosure of Henry et al. is concerned with permanent delivery of a drug across skin such that it can be systemically delivered. The disclosure of Chan et al. is concerned with transient, local replacement of an intracellular fluid with a biocompatible fluid for the purpose of temporarily reducing light attenuation at the tissue site of delivery. Not surprisingly, nowhere do Henry et al. teach or suggest that the Henry microneedle drug delivery system could be used to deliver a clarifying agent to skin to temporarily enhance the optical transparency thereof.

Because there is no disclosure in Henry et al. that would motivate one of ordinary skill in the art to combine the Henry et al. systemic drug delivery disclosure with the Chan et al. local replacement fluid delivery disclosure, and because the two references are concerned with two distinct and different problems, the references provide no motivation for one of ordinary skill in this art to combine them to reach the invention of present claim 30. Applicant submits that the present claims are patentable under 35 U.S.C. 103(a) in view of Chan and Henry.

For the reasons stated above, Applicant respectfully submits that present claims 17-31 are patentable under 35 U.S.C. 103(a) in light of Chan et al. and Edwards, Weaver et al., and/or Henry et al.

Request for an Interview

Should there by any remaining issues after entry of the amendment and consideration of the remarks herein, Applicants respectfully request either an in-person interview or a telephonic interview with the Examiner.

Extension of Time

A Petition for an Extension of Time for two months under 37 C.F.R. §1.136 and the appropriate fee has been filed to extend the due date for responding to the Official Action to 1 March 2003.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. **06-1358**, referencing Attorney Docket No. **P66960US1.**

Respectfully submitted,

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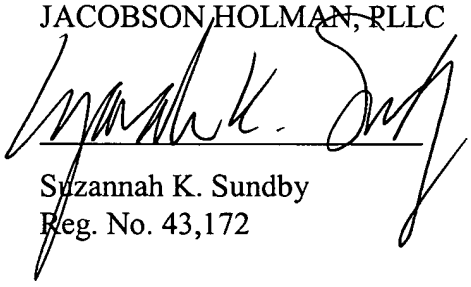

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